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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR,

Declaration under Rule 4.17:

— *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *with international search report*
— *before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments*

(88) Date of publication of the international search report:

16 June 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ADMINISTRATION OF DENDRITIC CELLS PARTIALLY MATURED *IN VITRO* FOR THE TREATMENT OF TUMORS

(57) Abstract: The present invention provides populations of cells comprising partially matured dendritic cells that can be used for administration individuals having a tumor. Partially matured dendritic cells, those contacted with a dendritic cell maturation agent for about 1 to about 10 hours, or more, efficiently take up and process tumor antigens in the area of the tumor site, complete maturation, and can subsequently migrate to the lymph nodes of a treated individual. Once in the lymph node the now fully mature antigen presenting dendritic cells secrete the appropriate cytokines (e.g., TNF α and IL-12) and contact T cells inducing a substantial anti-tumor immune response.

PATENT COOPERATION TREATY

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| | | |
|---|--|---|
| Applicant's or agent's file reference | FOR FURTHER ACTION | see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. |
| International application No. PCT/US03/38672 | International filing date (<i>day/month/year</i>) 12 May 2003 (12.05.2003) 5 December 2003 (05.12.2003) | (Earliest) Priority Date (<i>day/month/year</i>) 12 June 2002 (12.06.2002) 6 December 2002 (06.12.2002) |
| Applicant NORTHWEST BIOTHERAPEUTICS, INC. | | |

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 2 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (See Box II).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/38672

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 35/002; C12N 5.00+, 5/02
 US CL : 435/325,372,375,384; 514/291; 424/577

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/325,372,375,384; 514/291; 424/577

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 MEDLINE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | NESTLE, F.O. Dendritic cell vaccination for cancer therapy. Oncogene. 2000, Vol. 19, pages 6673-6679, see entire document. | 1-6 |
| y | TSUJI et al. Maturation of human dendritic cells by cell wall skeleton of Mycobacterium bovis Bacillus Calmette-Guerin: involvement of toll like receptors. Infection and Immunity. 2000, Vol.68, pages 6883-6890 | 6-9 |
| Y | US 6,558,951 B1 (TOMAI et al) 11 February 1999(11.02.1999), column 2, lines 32-37 and column 13, lines 59-66. | 6,10,11 |
| Y | KADOWAKI et al. Distinct CpG DNA and polyinosinic-polycytidilic acid double stranded RNA, respectively stimulate CD 11c- type 2 dendritic cell precursors and CD 11+ dendritic cells to produce type I IFN. The Journal of Immunology. 2001, Vol.166, pages,2291-2295, especially abstract, Figs. 2,3 | 6,12 |
| Y | TJOA et al. Dendritic cell-based immunotherapy for prostate cancer. CA Cancer J Clin. 1999, Vol.49, pages 117-128, see entire document | 13-32 |

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

03 April 2005 (03.04.2005)

Date of mailing of the international search report

22 APR 2005

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
 Commissioner of Patents
 P.O. Box 1450
 Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Jeffrey Siew

Telephone No. 571-272-1600

Form PCT/ISA/210 (second sheet) (July 1998)

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PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
POOR, BRIAN, W.
TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero center, 8th Flr.
San Francisco,, CA 94111

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

| | | |
|---|--|--|
| 020093-004010PC | | Date of Mailing (day/month/year) 22 APR 2005 |
| Applicant's or agent's file reference | FOR FURTHER ACTION See paragraphs 1 and 4 below | |
| International application No. PCT/US03/38672 | International filing date (day/month/year) 12 May 2003 (12.05.2003) 5 December 2003 (05.12.2003) | |
| Applicant NORTHWEST BIOTHERAPEUTICS, INC. | | |

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34, chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90 *bis*.1 and 90 *bis*.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

| | |
|--|--|
| Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230 | Authorized officer Jeffrey Siew Telephone No. 571-272-1600 |
|--|--|

Form PCT/ISA/220 (April 2002)

(See notes on accompanying sheet)

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